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**Multomic profiling of the rat nucleus accumbens reveals cell-type specific chromatin remodeling and transcriptional alterations after cocaine experience**

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Cocaine use elevates dopamine levels in the nucleus accumbens (NAc) to initiate cell-signaling cascades that engage transcriptional machinery and promote long-lasting synaptic and behavioral adaptations. Enduring drug-induced changes in gene expression in the NAc are thought to be mediated in part by chromatin reorganization within cocaine-affected cell populations. Prior studies using epigenetic profiling of bulk NAc tissues have identified widespread changes in chromatin-associated proteins, histone modifications, and DNA methylation following cocaine experience. However, little is known regarding how cocaine alters chromatin dynamics in a cell-type specific manner within the NAc, or whether these changes persist after cessation of drug use. Here, we used a cocaine self-administration model to profile long-lasting chromatin and transcriptional alterations induced by volitional cocaine use with single-cell resolution in a rat model system. Multomic profiling with single-nucleus RNA sequencing (snRNA-seq) and single-nucleus Assay for Transposase Accessible Chromatin (snATAC-seq) on 39,325 nuclei from the rat NAc after 30 days of withdrawal confirmed perviously identified neuronal and non-neuronal cell types in the NAc. Comparison of accessible chromatin regions between annotated cell types revealed thousands of cell-selective regulatory elements, many of which are linked to genes previously implicated in substance use disorders and motivated behaviors. Moreover, this dataset revealed enduring and cell-specific chromatin alterations present after 30 days of cocaine withdrawal. These results provide key insights into how cellular diversity contributes to chromatin and transcriptional alterations following cocaine experience, and suggest the importance of cell-type specific genomic regulation in substance use disorders.